Author’s response to reviews

Title: A novel mutation of WFS1 gene in a Chinese patient with Wolfram syndrome: a case report

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Version: 1 Date: 13 Jul 2017

Author’s response to reviews:

Dear editors and reviewers:

Thank you very much for your letter and we greatly appreciate your efforts to have the manuscript ‘A novel mutation of WFS1 gene in a Chinese patient with Wolfram syndrome: a case report’ (ID: BPED-D-17-00294) reviewed. Additionally, we would also like to thank the reviewers for the helpful and constructive comments. Those comments are all valuable and very helpful for revising and improving our paper. We have studied reviewers’ comments carefully and have tried our best to make revisions which marked in red in the paper. We hope that the revisions could make our article more acceptable.

Sincerely,

Yours,

Min Li
The responds to the reviewers’ comments are as following:

Reviewer 1

I read with great interest the manuscript number BPED-D-17-00294 entitled "A novel mutation of WFS1 gene in a Chinese patient with Wolfram syndrome with literature review". Aim of this case report is to firstly report a novel mutation c.1760G>A in Wolfram syndrome 1 (WFS1) gene, located on chromosome 4p16.1, in a 11-year-old Chinese boy.

A thorough English language revision is needed: i.e. needed: i.e. the last sentence of Background section is grammatically incorrect (page 2, lines 8-9).

Responds:

We are very sorry for our incorrect writing. It is a very important problem, we would try our best to revise it.

The section on the Case Presentation is too poor in clinical information, which is essential for clinical diagnosis of tungsten syndrome and lead to generic investigation. There is little information given about the onset of type 1 diabetes, its clinical and biochemical characteristics. Only information on instrumental exams and antibody tests is provided. Interesting, of course, is the description of a new mutation, which however needs to be integrated in detail with clinical, biochemical, and therapeutic information.

Responds:

We greatly appreciate Reviewer for this question. This evaluation is very valuable. Here was more information about the patient’s onset of T1DM. The patient’s mother recalled that he was polydipsia, polyphagia and polyuria and with weight loss for one month. He fainted suddenly in school with finger point blood glucose test > 33.3 mmol/L, blood glucose 38mmol/L, HbAc 15.8%, positive urine sugar and ketone. He was treated with insulin pump of Medtronic in the local hospital. We have re-written the Case Presentation section according to the reviewer’s suggestion.

Special thanks to you for your good comments.
Reviewer 2

In this paper the authors describe a patient with a novel WFS1 mutation. The paper is interesting but some points could be improved.

1. In the title, it seems that the authors review the literature. In my opinion the literature review is quite limited. Could you change the title?

Responds:

It is really true as Reviewer suggested that. And we have changed the title into ‘A novel mutation of WFS1 gene in a Chinese patient with Wolfram syndrome: a case report’.

2. Please, report some information about blood glucose control, diabetes treatment, biochemistry at diabetes onset.

Responds:

Great minds think alike. We greatly thank Reviewer 2 for this question as Review 1. We have re-written the Case Presentation section considering the reviewer’s suggestion.

3. Did you assess hearing function?

Responds:

It is a valuable question. Physical examinations of the nervous system have been done in our hospital, there was no obvious abnormality in the initial examination of hearing. Hearing tests performed in the local hospital were normal, but we could not provide the original data. The patient’s father refused to review the hearing function in our hospital.

4. The authors claim this is a novel mutation. I think that they should state which mutation database was used to assess that this is a novel mutation and how they can say it is a causative
one rather than a polymorphism. It cosegregates with phenotype, but an in silico analysis or something like that would improve its reliability.

Responds:

We really appreciate Reviewer for this helpful question. This is a very good question. We used the Human Gene Mutation Database (HGMD) to assess that this was a novel mutation. WFS1/wolframin spanning approximately 33.4 kb of genomic DNA on chromosome 4p16.1, consists of eight exons. The majority of the WFS1 mutations are concentrated in the exon 8. The boy in this case started with T1DM and OA, which were typical clinical features of WS. The patient’s number 587 codon c.1760G>A, located in exon 8, mutated and changed from arginine to glutamine. He was homozygote while his parents were both heterozygote of mutant genes without any signs or symptoms of WS. No genotype-phenotype correlation has been identified yet [1]. So we concluded that the novel mutation of the WFS1 gene contributed to the disease.

Thank you very much for your comments and suggestions.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in red in revised paper. We appreciate for editors/reviewers’ warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.